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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,885	12/18/2001	Jaime Simon	44142B	3197

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THE DOW CHEMICAL COMPANY
INTELLECTUAL PROPERTY SECTION
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EXAMINER
HARTLEY, MICHAEL G

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,885	SIMON ET AL.	
	Examiner	Art Unit	
	Michael G. Hartley	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2,3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 1, the definition of "X" as "a group that is negatively or positively charged at physiological pH" was not described in a reasonably generic manner to show that applicant had possession of this generic definition. For example, there are an almost unlimited number of chemical and biochemical moieties which could be negatively or positively charged as physiological pH (e.g., which itself may vary). This generic definition includes small organics, as well as, various macromolecules, e.g., large carbohydrates, peptides, negatively charged lipids or phospholipids, etc. Clearly, all these chemical moieties were not envisioned as being group "X" by applicant at the time of filing, since this definition encompasses an almost unlimited number of chemical substituents. This is supported since applicant defines "X" only to include only small organic groups, e.g., "X groups are primary amines, which may be secondary, tertiary, quaternary or sulfonates" on page 10 of the specification.

The dependent claims fall therewith. NOTE: Inserting the definition of X from claim 2 into claim 1 will obviate this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the recitation of "a group that is negatively or positively charged at physiological pH" is indefinite because it is not clear what all groups are encompassed thereby. Since this would depend on both the exact chemical structure of the moiety and the exact pH thereof, it is not clear what all groups would be encompassed by this recitation. This is not an art recognized term, and while the specification provides a few examples thereof, it fails to define the generic terminology of X, as claimed, to provide a clear understanding thereof. The dependent claims fall therewith. NOTE: Inserting the definition of X from claim 2 into claim 1 will obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoechst (GB 1391918).

Hoechst discloses a pharmaceutical formulation comprising a radiolabeled compound of formula (II), see page 1, column 2. This formula includes compounds which are within the scope of those claimed, note, one X and Y are hydroxyl and the other is radioactive iodine and the amine group is encompassed by X, see page 1, column 2. The compounds include methyltyrosine, see examples.3-6. The radioiodinating provides wherein at least 90% of the iodide has been exchanged, see page 2, columns 1 and 2. Hoechst discloses that various aqueous pharmaceutical carriers may be used, see page 3.

Claims 1, 2, 6-9, 11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Krummeich (Appl. Radiat. Isot., Vol. 46, No.9, 1995, PTO-1449).

Krummeich discloses a formulation comprising a compound of formula 1-3, see scheme 1 on page 918. This formula includes compounds which are within the scope of those claimed, e.g., the amine encompasses X and the carboxyl group corresponds to an R group. The compounds are contained in aqueous buffers which are pharmaceutically acceptable, and would provide the compounds in the chloride salt forms, see page 917.

Claims 1, 2, 6, 10, 11, 17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gavras (US 4,574,079).

Gavras discloses a pharmaceutical formulation comprising a radiolabeled compound of formula (I), see column 2. This formula includes compounds that are within the scope of those claimed, note, one X and Y are hydroxyl and the other is radioactive iodine, while the substituent at the 1 position includes those which would have a charge at physiological pH (e.g., contains an amine which corresponds to X as claimed, and a carboxyl corresponding to an R group as claimed). The formulations include pharmaceutically acceptable media (e.g., water), see column 7, lines 26+. Also, the compounds are present wherein at least 96% of the iodide has been exchanged, see column 9, lines 3-7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2 and 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Hoechst (GB 1391918) or Krummeich (Appl. Radiat. Isot., Vol. 46, No.9, 1995, PTO-1449) or Gavras (US 4,574,079) in view of Shochat (US Pat. 5,961,955) and Snyder (US Pat. 4,197,288).

Hoechst, Krummeich and Gavras all disclose formulations comprising radioiodinated compounds, as set forth above.

Hoechst, Krummeich and Gavras fail to disclose the addition of HEPES buffer and a radiolytic protectant in the pharmaceutically acceptable carrier as claimed. Further, Krummeich, while disclosing I-123, fails to teach I-125.

However, both Hoechst and Gavras teach the equivalence of I-125 and I-123.

Shochat discloses radiopharmaceutical compositions, wherein the addition of stabilizers (e.g., ascorbate) imparts enhanced radioprotection of radiopharmaceutical compositions, see columns 3-4.

Snyder teaches that HEPES buffer is a well known buffer which may be used for radiopharmaceuticals containing iodine isotopes to impart a preferred pH of 6 to 9, see column 5, lines 14+.

It would have been obvious to one of ordinary skill in the art to modify the methods disclosed by any one of Hoechst, Krummeich and Gavras to add a stabilizer to the composition because it is well known in the art that the addition of stabilizers (e.g., ascorbate) imparts enhanced radioprotection of radiopharmaceutical compositions, as shown by Shochat. Further, it would have been obvious to use HEPES as the buffer in the compositions used in the methods disclosed by Hoechst, Krummeich and Gavras because HEPES is a buffer which is known to be useful for radiopharmaceuticals to provide a desired pH in the range of 6 to 9, as taught by Snyder. Also, it would have been obvious to use either I-123 or I-125 as the radioiodine in the compounds disclosed by Krummeich because these radioisotopes are clearly known in the art as equivalents as shown by Hoechst and Gavras.

Conclusion

Claims 3-5 are free of the art of record. The prior art fails to teach or suggest formulations comprising compounds having a formula as set forth in these claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-

2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Michael G. Hartley
Primary Examiner
Art Unit 1616

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